REMARKS

Finality of the Office Action

Patent Application Information Retrieval (PAIR) records indicate that the present Office Action, which is a second action on the merits, is a final Office Action. This contradicts with the "Status" section at page 2 of the outstanding Office Action, wherein it is expressly stated that the present action is non-final.

Status

1)☒ Responsive to communication(s) filed on *28 December 2009*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

The conclusion section of the Office Action (see page 24) also does not identify the action being final (e.g., using form paragraph ¶7.40), as per the guidelines under MPEP §706.07(a). Correction thereof is earnestly solicited.

Claims

Claims 13, 15, 21, 22, 26, 30, 31, 33, 35 and 36 are currently under examination pursuant to the restriction requirement mailed August 24, 2007 and May 28, 2009.

Claims 1–12 and 16 have been withdrawn from consideration pursuant to the aforementioned restriction and election requirements.

Claims 14, 17–19, 20, 23–25, 27–29, 32 and 34 were previously cancelled without prejudice or disclaimer.

Claims 37 and 38 are added by this paper.

Claim amendments

Newly added claim 37 is directed to polypeptides of the instant invention consisting of the sequences set forth under SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6 or a polypeptide variant of SEQ ID NO: 2 having the amino acid variations set forth in clones 1-11. Claim 38 is directed to N-terminal (1-200) or C-terminal (185-500) fragments of the polypeptides of the instant invention (e.g., polypeptide consisting of the sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6 or a polypeptide variant of SEQ ID NO: 2 comprising amino acid variations are set forth in clones 1–11).

It is respectfully submitted that the amendments presented herein do not raise new matter. Entry thereof is earnestly solicited.

IDS

Applicant notes that the citations of articles by Suck et al. (*Clin Exp Allergy*. 2000, vol. 30, 324-32 "Suck I"; *Clin Exp Allergy*. 2000, vol. 30, pages 1395-402; "Suck II") along with Stomvoll et al. and Fahlbusch et al. were crossed-out from the PTO-1449 form filed on December 3, 2007. Copies of references are enclosed herewith for the Examiner's review.

Rejections under §102(b)

Rejections over Suck et al. (*Clin Exp Allergy*. 2000, vol. 30, 324-32 "Suck I") and/or (*Clin Exp Allergy*. 2000, vol. 30, 1395-402; "Suck II")

Under item 11 of the Office Action, the Examiner alleges that claims 13, 15, 21, 22, 26, 30, 31, 33 and 35-36 are anticipated by Suck et al. (*Clin Exp Allergy*. 2000 Mar;30(3):324-32). Under item 9 of the Office Action, the Examiner further alleges that the same claims are anticipated by Suck et al. (*Clin Exp Allergy*. 2000 Oct;30(10):1395-402). These rejections are respectfully traversed.

With respect to natural Phl p4 identified in Fig. 4 of the "Suck I" reference , Applicant submits that the referenced nPhl p4 is different from the polypeptides of the instant invention. To this end, the Examiner's attention is directed to the 1st complete paragraph of col. 1 at page 325 of "Suck I", wherein it is expressly stated that "Phl p 4 with a molecular mass of 55 kDa is modestly described as a basic and trypsin-resistant glycoprotein [9]." In the subsequent "SUCK II" publication, the same clone was used. In particular, in the paragraph bridging cols. 1 and 2 at page 1396 of SUCK II, it is explicitly stated that "Phl p 4 was purified according to the procedures of Haavik et al. [6] and Fischer et al. [7]." Thus the Phl p 4 protein of the referenced "SUCK I" and "SUCK II" relates to the previously-cited disclosure by Fischer et al. (*Journal of Allergy and Clinical Immunology*, 98, 189-198, 1996; PUBMED ID: 8765834; See REF [9] in SUCK I and REF [7] in SUCK II). As to Haavik et al. (REF [6] in SUCK II), please see *infra*.

In this article, Fischer teaches decapeptide sequence of Phl p 4 containing ten amino acid residues (IVALPXGMLK) of the N-terminal region of Phl p 4. See, Fig. 5 and the description thereof at page 194 of Fischer et al. The polypeptide by Fischer does not show any homology to the Phl p 4 amino acid sequences of SEQ ID NO: 2, 4 and 6. For example, Lipman-Pearson Alignment analysis and DotPlot analysis with LASERGENE (DNASTAR) merely showed single Phl p 4 regions with sequence identities in three positions. Such low values do not

indicate homology but random identities. See Exhibit A (SIM+LALNVIEW analysis). As such, it is clear that in view of Fischer et al., the polypeptides of Suck et al. are structurally distinct from the claimed polypeptides of SEQ ID NOs: 2, 4, and 6, including variants of SEQ ID NO: 2 having the amino acid variations set forth in clones 1–11. See claims 13 and 37.

Further enclosed herewith in Exhibit B is a CLUSTAL multiple sequence alignment between Fischer's Phl p 4 dodecapeptide and the instant sequence set forth in SEQ ID NOs: 2, 4 and 6. As can be seen, there is no structural similarity between the art-disclosed Phl p 4 sequence and the instant polypeptides. For example, the CLUSTAL score of similarity between the recited SEQ ID NOs: 2, 4 and 6 is greater than 92. By contrast, Fischer's Phl p 4 polypeptide only achieved a maximum score of 30. As such, Suck et al. in view of Fischer et al. fails to anticipate the instantly claimed polypeptides.

Claims directed to fragments and partial sequences

Insofar as the enclosed similarity analysis reveals that there is no stretch of amino acids in the art-disclosed Phl p 4 protein sequence and instantly claimed Phl p 4 polypeptides, the recited N-terminal and the C-terminal fragment sequences, along with partial sequences of 50 to 350 amino acids are also novel over Suck et al.

Withdrawal of the rejection is respectfully requested.

The rejection over Fahlbusch et al.

With respect to the disclosure in Fahlbusch et al. (*Clinical & Experimental Allergy*, 1998) and the §102(b) rejection based thereon, the Examiner's allegations are respectfully traversed. It appears that this rejection is based on the cited references' disclosure of the term Phl p 4 polypeptide. The Examiner is alleging that the references' teaching of Phl p 4 protein creates a presumption of structural identity. This contention lacks scientific merit. For example, with respect to Group 4 allergens, Fahlbusch expressly teaches that "Group 4 allergens were described as basic glycoproteins of 55-60 kDa molecular weight (mol. wgt.) with a pI of 9.4 in different grass species [5, 12, 13]. Recently Phl p 4 was characterized as a trypsin-resistant protein [14]." See the 1st complete paragraph of col. 1 at page 800 of the enclosed Fahlbusch et al. To this end, Applicants have reviewed the articles by Haavik et al. (REF [5]), Ekamadullah et al. (REF [12]), Brodard et al. REF [13]) and Fischer et al. (REF [14]) in the cited Fahlbusch et al. Ekamadullah and Brodard are not germane to the instant

invention as they are directed to unrelated *Lolium perene* Group 4 allergens and *Dactylis Glomerata* Group 4 allergens, respectively. Fischer et al. generically teaches Group 4 allergens from *Phleum pratense*; however, in view of the analysis provided in the preceding paragraphs, it is clear that the allergens of Fischer are structurally different from the Phl p 4 allergens of the instant application.

With respect to Haavik et al. (*Int Arch Allergy Appl Immunol.*,78(3):260-8, 1985), an ABSTRACT of the article is enclosed herewith for the Examiner's review. Haavik teaches pollen allergens from timothy II having a MW of "54,000 and 38,000 by SDS-PAGE and gel filtration, respectively" and "isoelectric point of 9.45." Haavik does not teach that these proteins are Group 4 allergens from *Phleum pratense*. Moreover, as is evidenced by Exhibit C enclosed herewith, Haavik's allerges are smaller and more basic than the instantly claimed polypeptides of SEQ ID NOs: 2, 4, and 6. For example, Compute pI/MW analysis (program freely available via EXPASY) of instant SEQ ID NOs: 2, 4, and 6 reveals that the allergens of the instant invention have a theoretic pI < 9.2 and a MW of ~56 kDa. Thus Fahlbusch in view of Haavik and/or Fischer also fails to anticipate the subject matter of the instant claims.

Applicants assert that the polypeptides of the instant application are novel over the totality of SUCK I, SUCK II and Fahlbusch et al. To this end, a search with the term "Phl p 4" in the allergen nomenclature (AN) database revealed three hits. Results are enclosed herewith for the PTO's review. See, Exhibit D. The first hit (allergenicity reference: 1597349) does not provide any sèquence information and only indicates that the allergen is a 55 kDa protein. The reference protein leads to an article by Valenta et al. (*Int Arch Allergy Immunol.*, 97: 287-94, 1992) entitled "Diagnosis of grass pollen allergy with recombinant timothy grass (Phleum pratense) pollen allergens." Judging from the Valenta abstract, it seems that article only teaches activity of <u>different</u> Phl p **1** and Phl p **5** allergens from *Phleum pratense*.

The other two hits (Uniprot accession Nos. Q5ZQK4 and Q5ZQK5) from the AN database provide sequences of the allergens but point to Applicants' own **post-published** disclosure in BBRC (i.e., Nandy et al., BBCR 337 (2), 563-570 (2005)). These are not prior art.

Withdrawal of the rejection is respectfully requested.

<u>Alleged inherent anticipation</u>

It is by now well-established that "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See MPEP §2131 and further corroborated by the Fed. Circuit's decision in

Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 2 USPQ2d 1051 (Fed. Cir. 1987). With respect to inherency, the Courts have established that "the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999). Inasmuch as the cited Suck et al. and Fahlbush et al. say nothing about Phl p 4 polypeptide sequences and the art (or the Examiner) has not established that the Phl p 4 polypeptide disclosed therein necessarily comprises the sequences recited herein, the rejection is without legal merit.

With respect to the PTO's contention that sequences need not be provided, the controlling case law dictates that for anticipation, "the identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 9 USPQ2d 1913 (Fed. Cir. 1989). The Office Action fails to establish that the polypeptides disclosed in the aforementioned references contain the **complete** Phl p 4 polypeptide sequence as presently claimed. To this end, the enclosed Exhibit B unequivocally demonstrates that it cannot be ascertained whether the references teach a sequence that is completely identical to what is claimed in the present application. More importantly, it is clear to those skilled in the art that none of the cited references of Suck et al. and Fahlbusch et al. provide "a complete detail" (i.e., the polypeptide sequence) of the claimed invention. As such, an inherency rejection under §102/§103 is not supported and should be withdrawn. See MPEP §2112.

Moreover, the Examiner has given no basis for alleging that it would be "reasonable" to assume that the references' products are the same as those claimed herein. See *In re Best* 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). If anything, the record summarized above shows such as assumption to be unreasonable. Thus, the burden remains on th Examiner. Withdrawal of the rejection is respectfully requested.

Claims directed to recombinant polypeptides

In view of Applicants' own disclosure, for example, Fig. 4 of the instant specification, it is clear that the recombinant polypeptides of the instant invention are different and thus novel over the natural Phl p 4 polypeptides. Therein, it is expressly disclosed that nPhl p 4 has a higher molecular weight than r Phl 4 of the instant invention. Favorable reconsideration is

respectfully requested.

Rejection under 35 U.S.C. §112, ¶1

Claims 21, 22, 30 and 31 are rejected under this section for allegedly failing to comply with the enablement requirement. Claim 21 is rejected under this section for allegedly failing to provide adequate written description. Applicants respectfully traverse these rejections.

With regard to the written description rejection, Applicants submit that in view of the Examiner's arguments at page 9 of the Office Action, the subject matter of claims 13 and 22, including newly added claims 37 and 38 is adequately described.

With regard to the enablement rejection, the Office Action contends that specification does not provide enablement for the fragment polypeptides recited in claim 22 and/or the functional activity of such partial sequences recited in claim 21. The Examiner further contends that the pharmaceutical preparations comprising such fragments or partial sequences are not enabled.

Applicants remarks of December 28, 2009 are incorporated by reference in their entirety with regard to the sustained rejections under §112, ¶1.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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